HETEROCYCLES, Vol. 3, No. 9, 1975

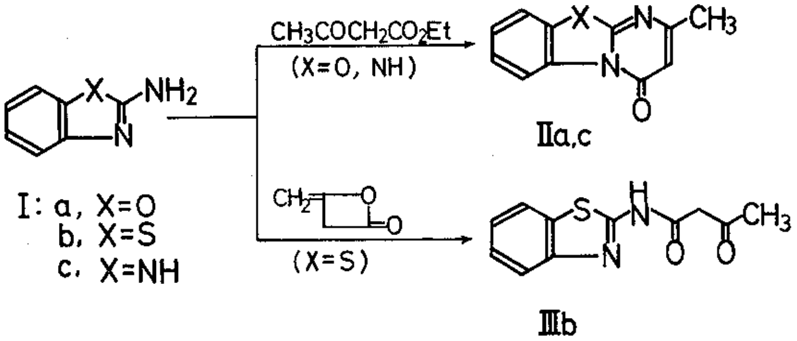
Reaction of 2-Aminobenzoxazole with Diketene[1)]

Tetsuzo Kato, Takuo Chiba and Mohsen Daneshtalab
Pharmaceutical Institute, Tohoku University, Aobayama,
Sendai 980, Japan

2-Aminobenzoxazole reacts with diketene to give the related N-acetoacetyl, and pyrimido-[1,2-a]benzoxazol-4-one derivatives in good yield. Ring closure reaction of the N-acetoacetyl derivative (IIIa), and other reactions are described.

Antaki et al.[2)] reported that 2-aminobenzoxazole (Ia, X=O) and 2-aminobenzimidazole (Ic, X=NH) reacted with ethyl acetoacetate to give 2-methyl-4H-pyrimido[2,1-b]benzoxazol-4-one (IIa, X=O) and 2-methyl-4H,10H-pyrimido[1,2-a]benzimidazol-4-one (IIc, X=NH), respectively. Ried et al.[3)] reported the similar reaction of 2-aminobenzimidazole (Ic) with β-diketones to give the pyrimido[1,2-a]-benzimidazole derivatives. On the other hand, Allen et al.[4)] investigated the reaction of 2-aminobenzothiazole (Ib, X=S) with diketene, and obtained 2-acetoacetamidobenzothiazole (IIIb) in quantitative yield.

While investigating on some potential uses of diketene, our interest was focused on the reaction of 2-aminobenzoxazole (Ia) and 2-aminobenzimidazole (Ic) with diketene, which is the subject of the present paper.

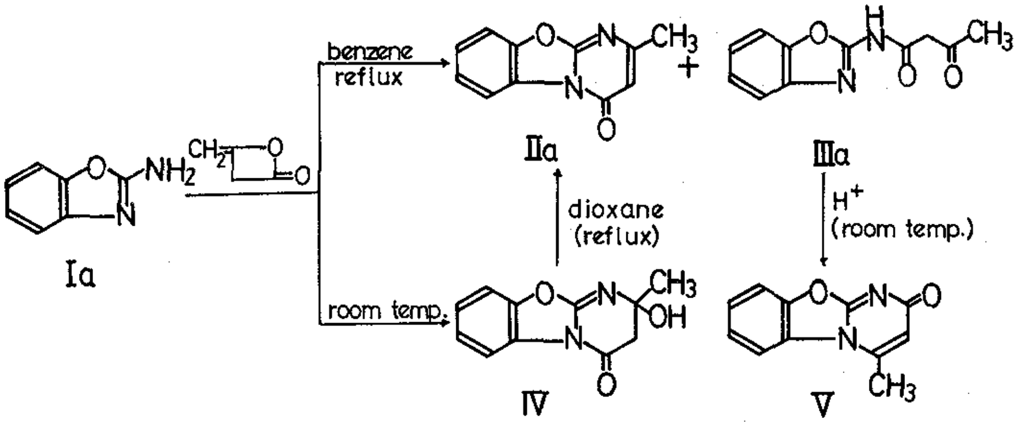


A mixture of 2-aminobenzoxazole and a slight excess of diketene in benzene was refluxed for 2 hr, and condensed in vacuo to give an oily residue, which was purified by recrystallization from ether giving colorless prisms of mp 144-145° (lit. mp 146°$^{2)}$), $C_{11}H_8O_2N_2$ (IIa), in 17% yield. The residual solid insoluble in boiling ether was recrystallized from benzene to give colorless prisms of mp 138-139°, $C_{11}H_{10}O_3N_2$ (IIIa), in 23% yield.

The ir and nmr spectral data of IIa and IIIa are as follows: IIa, ir $\nu_{max}^{CHCl_3}$ cm^{-1}: 3040, 1710 (sh), 1693, 1642, 1612, 1538. nmr ($CDCl_3$) ppm: 2.39 (3H, s,$-CH_3$), 6.20 (1H, s, C_3-H), 7.26-7.56 (3H, m, C_7,C_8,C_9-H), 8.20-8.48 (1H, m, C_6-H). IIIa; ir $\nu_{max}^{CHCl_3}$ cm^{-1}: 3440 (sh), 3240 (sh), 3025, 1725, 1705 (sh), 1625, 1585. nmr ($CDCl_3$) ppm : 2.05 (0.8H, s, $\underline{CH_3}$-C(OH)=C), 2.36 (2.2H, s,

CH_3-CO-), 3.92 (1.3H, s, -CH_2-), 5.82 (0.3H, br.s, -<u>CH</u>=C(OH)CH_3), 7.30-7.60 (5H, m, ring H, NH), 12.10-12.90 (0.4H, br, enol OH). Keto:enol=2.75:1.

Under the similar reaction condition, the use of 2-aminobenzoxazole (Ia) in excess resulted in the formation of IIIa in 46% yield. Reversely, in the case of the use of diketene in excess, IIa was afforded in 72% yield.



However, when the reaction was carried out at room temperature, the cyclic adduct (IV) was obtained. Namely, 2-aminobenzoxazole (Ia) was added in excess diketene with ice-cooling. The reaction mixture was stirred at room temperature until 2-aminobenzoxazole was completely dissolved, during which time an exothermic reaction was regulated with water-cooling. Crystals precipitated were collected, and purified by recrystallization from ether to give colorless needles of mp 95-96°, $C_{11}H_{10}O_3N_2$ (IV), in 59% yield.

ir $\nu_{max}^{CHCl_3}$ cm^{-1}: 3280 (br), 2990, 1720 (sh), 1706, 1478. nmr ($CDCl_3$) ppm : 1.64 (3H, s,-CH_3), 2.86 (2H, ABq, J=16.2 Hz,-CH_2-), 5.00-5.40 (1H, br,-OH), 7.02-7.30 (3H, m, C_7,C_8,C_9-H), 7.66-7.95 (1H, m, C_6-H). Refluxing of IV in dioxane gave IIa in 44% yield. On the basis of these data, the structure of IV was assigned as 2-hydroxy-2-methyl-2H-3,4-dihydropyrimido[2,1-b]benzoxazol-4-one.

Stirring a solution of 2-acetoacetamidobenzoxazole (IIIa) in 5% HCl at room temperature gave rise to colorless prisms (from acetone) of mp 284-286°, $C_{11}H_8O_2N_2 \cdot H_2O$ (V·monohydrate), in 36% yield. This was characterized as 4-methyl-2H-pyrimido[2,1-b]-benzoxazol-2-one on the basis of spectral data as follows: ir ν_{max}^{KBr} cm^{-1}: 3360-3080, 1730 (sh), 1675, 1620, 1608. nmr (CF_3CO_2H) ppm: 2.10 (3H, s,-CH_3), 6.14 (1H, s, C_3-H), 6.98-7.60 (4H, m, benzene ring H).

Reaction of 2-aminobenzimidazole (Ic) with diketene gave a sole product, which was identified as IIc by the comparison with an authentic specimen prepared from Ic and ethyl acetoacetate according to the literature.[2)]

REFERENCES

1) This makes part LXXVIII of "Studies on Ketene and its Derivatives".

2) H. Antaki and V. Petrov, J. Chem. Soc., 1951, 551.

3) W. Ried and W. Müller, J. Prakt. Chem., 1954, **8**, 132.

4) C. F. H. Allen, J. van Allen, and C. V. Willson, J. Amer. Chem. Soc., 1944, **66**, 1805.